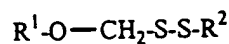


What is claimed is:

1. A hydrocarbyldithiomethyl-modified compound comprising the Formula:



or a salt thereof, wherein

- 5  $R^1$  is an organic molecule; and  
 $R^2$  is a hydrocarbyl.

2. The compound of claim 1 wherein said  $R^2$  comprises a fluorescent labeling group.

- 10 3. The compound of claim 2 wherein said fluorescent labeling group is selected from the group consisting of bodipy, dansyl, fluorescein, rhodamin, Texas red, Cy 2, Cy 4, and Cy 6.

- 15 4. The compound of claim 1 wherein said  $R^1$  further comprises at least one hydroxyl group that is not hydrocarbyldithiomethyl-modified.

5. The compound of claim 1 wherein said  $R^1$  is selected from the group consisting of modified or unmodified amino acids, peptides, proteins, carbohydrates, sterols, or steroids.

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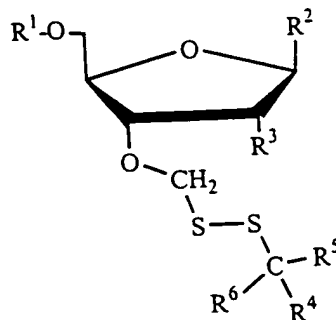
6. The compound of claim 5 wherein said  $R^2$  comprises a labeling group.

7. The compound of claim 5 wherein said  $R^1$  further comprises at least one hydroxyl group that is not hydrocarbyldithiomethyl-modified.

25

8. The compound of claim 1 wherein said  $R^1$  is selected from the group consisting of ribonucleosides, ribonucleotides, base- and/or sugar-modified ribonucleosides, base- and/or sugar-modified ribonucleotides, deoxyribonucleosides, deoxyribonucleotides, base- and/or sugar-modified deoxyribonucleosides, and base- and/or sugar-modified  
30 deoxyribonucleotides.

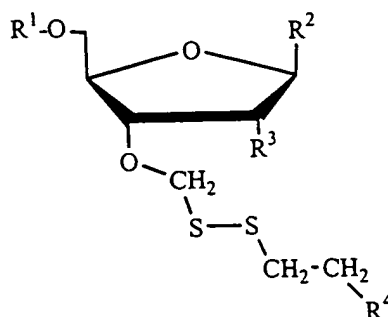
9. The compound of claim 8 wherein said  $R^2$  comprises a labeling group.
10. The compound of claim 8 wherein said  $R^1$  further comprises at least one hydroxyl group that is not hydrocarbyldithiomethyl-modified.
- 5 11. The compound of claim 8 wherein said hydrocarbyldithiomethyl modification is at a 3' hydroxyl position of said  $R^1$ .
12. The compound of claim 8 wherein said hydrocarbyldithiomethyl modification is at a 5' hydroxyl position of said  $R^1$ .
- 10 13. The compound of claim 8 wherein said  $R^1$  is selected from the group consisting of ribonucleosides, ribonucleotides, base- and/or sugar-modified ribonucleosides, and base- and/or sugar-modified ribonucleotides, and wherein said hydrocarbyldithiomethyl modification is at a 2' hydroxyl position of said  $R^1$ .
- 15 14. The compound of claim 1 wherein said  $R^2$  comprises an electron donating or withdrawing function.
- 20 15. The compound of claim 14 wherein said electron donating or withdrawing function contains a heteroatom selected from the group consisting of oxygen, nitrogen, sulfur, and silicon.
16. A hydrocarbyldithiomethyl-modified compound comprising the formula:



25

or a salt thereof, wherein

- $R^1$  is H, a protecting group, phosphate, diphosphate, triphosphate, or residue of a nucleic acid;  
 $R^2$  is a nucleobase;  
 $R^3$  is H, OH, or a protected form of OH; and  
5  $R^4$ ,  $R^5$  and  $R^6$  are together or separately H, hydrocarbyl, or a residue of a solid support.
17. The compound of claim 16 wherein  $R^4$ ,  $R^5$  and  $R^6$  together or separately further comprise a labeling group.
- 10 18. The compound of claim 16 wherein  $R^4$ ,  $R^5$  and  $R^6$  comprise together or separately an electron donating or withdrawing function.
19. The compound of claim 18 wherein said electron donating or withdrawing function contains a heteroatom selected from the group consisting of oxygen, nitrogen,  
15 sulfur, and silicon.
20. The compound of claim 16 wherein  $R^4$ ,  $R^5$  and  $R^6$  are together or separately H, methyl, ethyl, isopropyl, t-butyl, phenyl, or benzyl and wherein either  $R^4$ ,  $R^5$  or  $R^6$  is modified with a labeling group.
- 20 21. A compound comprising the Formula:



- or a salt thereof, wherein  
25  $R^1$  is H, a protecting group, a phosphate, diphosphate, or a triphosphate, or a residue of a nucleic acid;

$R^2$  is a nucleobase;

$R^3$  is H or OH, or a protected form of OH; and

$R^4$  is H or hydrocarbyl.

5     22.     The compound of claim 21 wherein  $R^4$  is modified with a labeling group.

23.     The compound of claim 21 wherein  $R^4$  comprises nitrogen.

24.     The compound of claim 21 wherein  $R^4$  is covalently linked to a solid support.

10

25.     A method for modifying a nucleoside comprising the steps of:

        a)     contacting a nucleoside having at least one hallogenomethyl-modified  
hydroxyl group with a thiosulfonate compound thereby forming a thiosulfonated  
nucleoside; and

15          b)     contacting said thiosulfonated nucleoside with a hydrocarbylthiol  
compound thereby forming a hydrocarbyldithiomethyl-modified nucleoside.

26.     The method of claim 25 wherein said thiosulfonate compound is selected from the  
group consisting of alkylthiosulfonate and arylthiosulfonate.

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27.     The method of claim 25 further comprising the step of labeling said  
hydrocarbyldithiomethyl-modified nucleoside.

28.     A method for sequencing a nucleic acid comprising the steps of:

25          a)     contacting a target nucleic acid with a primer under conditions wherein  
said primer anneals to said target nucleic acid in a sequence specific manner and wherein  
at least a portion of said primer is complementary to a portion of said target nucleic acid;

        b)     incorporating a hydrocarbyldithiomethyl-modified nucleotide into said  
primer; and

30          c)     detecting incorporation of said hydrocarbyldithiomethyl-modified  
nucleotide, wherein said hydrocarbyldithiomethyl-modified nucleotide is complementary

to said target nucleic acid at said hydrocarbyldithiomethyl-modified nucleotide's site of incorporation thereby identifying the sequence of one nucleobase of said target nucleic acid.

5 29. The method of claim 28 wherein said incorporating step is catalyzed by a DNA polymerase.

30. The method of claim 28 wherein said sequencing method is selected from the group consisting of minisequencing and sequencing by synthesis.

10

31. The method of claim 28 wherein said method is effective for use with a sequencing array.

32. A method for sequencing a nucleic acid comprising the steps of:

15

a) contacting a target nucleic acid with a primer under conditions wherein said primer anneals to said target nucleic acid in a sequence specific manner and wherein at least a portion of said primer is complementary to a portion of said target nucleic acid;

b) incorporating a first 3'-hydrocarbyldithiomethyl-modified nucleotide into said primer;

20

c) detecting said incorporation of said first 3'-hydrocarbyldithiomethyl-modified nucleotide thereby identifying the sequence of a nucleobase of said target nucleic acid;

d) removing said hydrocarbyldithiomethyl group from said first incorporated hydrocarbyldithiomethyl-modified nucleotide to form a first elongated primer having a

25

free hydroxyl group;

e) incorporating a second 3'-hydrocarbyldithiomethyl-modified nucleotide into said first elongated primer; and

f) detecting said second hydrocarbyldithiomethyl-modified nucleotide  
thereby identifying the sequence of another nucleobase of said target nucleic acid,  
wherein said first 3'-hydrocarbyldithiomethyl-modified nucleotide and said second 3'-  
hydrocarbyldithiomethyl-modified nucleotide are complementary to said target nucleic  
5 acid at each said nucleotide's site of incorporation.

33. The method of claim 32 wherein said detecting steps are performed before  
removing said hydrocarbyldithiomethyl group.

10 34. The method of claim 32 wherein said detecting steps are performed after  
removing said hydrocarbyldithiomethyl group.

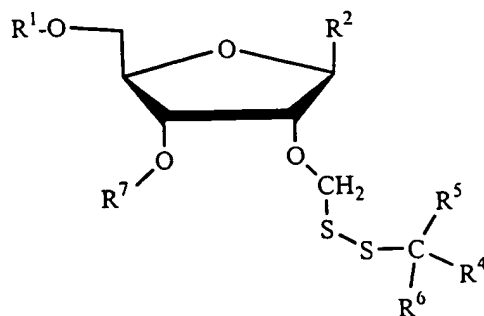
35. The method of claim 32 wherein said method is effective for use with a  
sequencing array.

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36. The method of claim 32 wherein steps a), b), c), d), e), and f) are performed under  
conditions that do not disrupt the annealing of said primer to said target nucleic acid.

37. A compound comprising the Formula:

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wherein

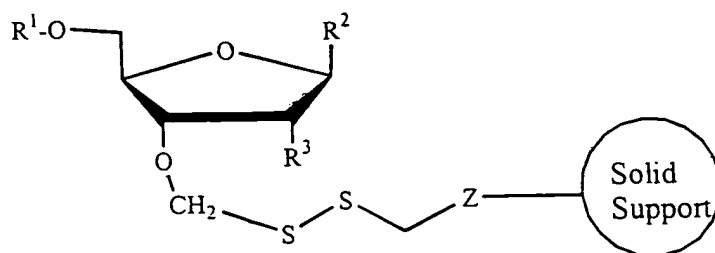
R¹ is a H, a protecting group, a phosphate, diphosphate, or a triphosphate, or a residue of  
a nucleic acid;

25 R² is a nucleobase;

$R^4$ ,  $R^5$  and  $R^6$  are together or separately H or hydrocarbyl; and  
 $R^7$  is H, H-phosphonate or phosphoramidite.

38. An oligonucleotide synthesis support comprising the formula:

5



wherein

$R^1$  is H, phosphate, diphosphate, triphosphate, or a protecting group,

$R^2$  is a nucleobase,

10  $R^3$  is H, OH, or a protected form of OH, and

Z is a group effective for covalent attachment to a solid support, said solid support being effective for covalently bonding an oligonucleotide during oligonucleotide synthesis.

39. The support of claim 38 wherein said Z is selected from the group consisting of  
15 amino, amide, ester, and ether.

40. A method for synthesizing an oligonucleotide comprising the steps of:

- a) providing a 5' protected first nucleoside covalently bonded to a solid support through a linker;
- 20 b) deprotecting said first nucleoside at its 5' position;
- c) covalently bonding another 5' protected nucleoside to said first nucleotide at the 5' position of said first nucleoside;
- d) deprotecting said another nucleoside at its 5' position; and
- e) repeating steps c) and d) for adding additional protected nucleosides, said
- 25 linker securing said first nucleotide to said solid support via a hydrocarbyldithiomethyl bond.

41. The method of claim 40 wherein said method is optimized for use in an array.

42. The method of claim 40 wherein said method is effective for inverting said  
oligonucleotide thereby forming an oligonucleotide having a free 3' hydroxyl and being  
5 covalently linked to a solid support.

43. The method of claim 42 wherein said method is optimized for use in an array.

44. The method of claim 40 further comprising the step of cleaving said  
10 oligonucleotide from said solid support.

45. A method for synthesizing an oligoribonucleotide comprising the steps of:

- a) providing a first protected ribonucleoside covalently bonded to a solid support;
- 15 b) covalently linking at least one 2'-hydrocarbyldithiomethyl-modified ribonucleoside to said first ribonucleoside to form an oligoribonucleotide;
- c) partially de-protecting said oligoribonucleotide under acidic or basic conditions; and
- d) contacting said oligoribonucleotide with a reducing agent under neutral  
20 conditions thereby completely de-protecting said oligoribonucleotide, wherein said method is effective for preventing cleavage or migration of internucleotide phosphate bonds, and wherein said hydrocarbyldithiomethyl-modified ribonucleoside comprises a hydrocarbyldithiomethyl group bound at the 2' position of said hydrocarbyldithiomethyl-modified ribonucleoside.

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46. The method of claim 45 wherein the pH of said neutral conditions ranges from about 5 to about 9.

47. The method of claim 46 wherein said pH is about 7.

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48. The method of claim 45 wherein said method is effective for inverting said oligoribonucleotide thereby forming a solid phase bound oligonucleotide having a free 3' hydroxyl.

5 49. The method of claim 45 wherein said first protected ribonucleoside is secured to said solid support via a hydrocarbyldithiomethyl bond.

50. A method for sequencing a nucleic acid comprising the steps of:

- a) providing a primer array comprising a plurality of sequencing primers;
- 10 b) contacting a target nucleic acid with said primer array under conditions wherein said sequencing primers anneal to said target nucleic acid in a sequence specific manner thereby forming target-primer complexes between complementary portions of said sequencing primers and said target nucleic acid;
- c) incorporating a first 3'-hydrocarbyldithiomethyl-modified nucleotide into  
15 at least one sequencing primer portion of said target-primer complexes, said first 3'-hydrocarbyldithiomethyl-modified nucleotide being complementary to said target nucleic acid; and
- d) detecting said incorporation of said first 3'-hydrocarbyldithiomethyl-modified nucleotide, wherein said first 3'-hydrocarbyldithiomethyl-modified nucleotide  
20 is complementary to said target sequence at said first 3'-hydrocarbyldithiomethyl-modified nucleotide's site of incorporation.

51. The method of claim 50 further comprising the steps of:

- e) removing said hydrocarbyldithiomethyl group from said first incorporated  
25 3'-hydrocarbyldithiomethyl-modified nucleotide to form a first elongated target-primer complex having a free 3' hydroxyl group;
- f) incorporating a second hydrocarbyldithiomethyl-modified nucleotide into said first elongated target-primer complex; and
- g) detecting said second 3'-hydrocarbyldithiomethyl-modified nucleotide,  
30 wherein said second 3'-hydrocarbyldithiomethyl-modified nucleotide is complementary

to said target sequence at said second 3'-hydrocarbyldithiomethyl-modified nucleotide's site of incorporation.

52. The method of claim 50 wherein said detecting said incorporation step is  
5 performed before removing a hydrocarbyldithiomethyl moiety.

53. The method of claim 50 wherein said method is effective for producing a plurality of nucleotide sequences, said nucleotide sequences corresponding to overlapping nucleotide sequences of said target nucleic acid.

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54. The method of claim 51 wherein said step e) is performed under conditions that do not disrupt said target-primer complexes.

55. A method for synthesizing an oligonucleotide comprising the steps of:  
15 a) providing a 5' protected first nucleoside covalently bonded to a solid support through a hydrocarbyldithiomethyl containing linker;  
b) deprotecting said first nucleoside at its 5' position;  
c) covalently bonding another 5' protected nucleoside to said first nucleotide at the 5' position of said first nucleoside;  
20 d) deprotecting said another nucleoside at its 5' position;  
e) optionally repeating steps c) and d) for adding additional protected nucleosides thereby producing an oligonucleotide;  
f) optionally selectively cleaving a protecting group from said oligonucleotide thereby forming a partially deprotected oligonucleotide;  
25 g) selectively cleaving said hydrocarbyldithiomethyl containing linker; and  
h) isolating said partially deprotected oligonucleotide.

56. The method of claim 55 further comprising the step of modifying the 3' terminus of said oligonucleotide with a reactive or detectable moiety.

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57. The method of claim 55 wherein at least one of said 5' protected nucleosides comprises a hydrocarbyldithiomethyl moiety.